BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

As rescanning documents *will not* correct images, please do not report the images to the Image Problem Mailbox.

JP 9-274041

* NOTICES *

1.This document has been translated by computer. So the translation may not reflect the original precisely.

2.**** shows the word which can not be translated.
3.In the drawings, any words are not translated.

CLAIMS

[Claim(s)]
[Claim 1] In the measuring method of the antigen-antibody reaction matter which measures the pr determined antigen in the extracted blood, or the concentration of an antibody A surfactant is poured in and agitated into the extracted blood. into this liquid A stabilizing agent, The measuring method of the antigen-antibody reaction matter characterized by irradiating light at this liquid and measuring the aforementioned predetermined antigen in the aforementioned blood, or the concentration of an antibody based on the amount of transmitted lights after the antibody or antigen to the buffer solution, the aforementioned predetermined antigen, or an antibody pours in and agitates the latex liquid by which sensitization was carried out.
[Claim 2] A predetermined antigen is the measuring method of the antigen-antibody reaction matter according to claim 1 characterized by being C reactivity protein.
[Claim 3] The measuring device of the antigen-antibody reaction matter which measures the predetermined antigen in the extracted blood characterized by providing the following, or the concentration of an antibody The container which holds the extracted blood A pouring means to pour in each of the lat x liquid with which sensitization of the antibody or antigen to a surfactant, a stabilizing agent, the buff r solution, the aforementioned predetermined antigen, or an antibody was carried out to the blood in this container A churning means to agitate the liquid in the aforementioned container An optical irradiation means to irradiate light at the liquid in the aforementioned container, an amount detection means of transmitted lights to detect the amount of transmitted lights which penetrated the liquid among the light by this optical irradiation means, and a density measurement means to ask for the aforementioned predetermined antigen in the aforementioned blood, or the concentration of an antibody based on th light which this amount detection means of transmitted lights detected
[Claim 4] A predetermined antigen is the measuring device of the antigen-antibody reaction matter according to claim 3 characterized by being C reactivity protein.

[Translation done.]

* NOTICES *

1.This document has b en translated by comput r. So the translation may not reflect the original precisely.

2.**** shows the word which can not be translated.
3.In the drawings, any words are not translated.

DETAILED DESCRIPTION

[Detailed Description of the Invention]
[0001]
[Th technical field to which invention belongs] this invention relates to the method of measuring the matter which produces antigen-antibody reactions, such as C reactivity protein [in blood] (it is called below C-Reactive Protein; CRP), rheumatoid factor (RF), and antistreptolysin O (ASO), and the equipment to measure.
[0002]
[D scription of the Prior Art] There is latex condensation immunonephelometry as a measuring method of this kind of matter. It is indicated about the measuring method of the matter which an antigen-antibody reaction (immunoreaction) generally produces in JP,53-62826,A about this method, is indicated by JP,53-86015,A about the measuring method of CRP, and is indicated by JP,62-218866,A about the reagent us d for measurement of CRP. According to this latex condensation immunonephelometry, the concentration of the matter which produces an antigen-antibody reaction can be quantitatively measured with a sufficient precision.
[0003]
[Problem(s) to be Solved by the Invention] However, by this method, if the extracted blood (whole blood) is used as it is, it cannot be influenced of an erythrocyte, hemoglobin, etc. and exact fixed quantity measur ment cannot be performed. For this reason, in the conventional biochemical inspection, centrifugal separation of the blood extracted as mentioned above was carried out, the blood serum was taken, and it was measuring using this blood serum. For this reason, measurement was difficult in the institution which th m asuring time starts for a long time, and has neither the case of emergency, nor a centrifugal s paration machine. On the other hand, in order to have investigated the constituent of blood (the number of erythrocytes, and white blood cell count) of the extracted blood, it had taken time and effort very much that it must separate into the object for biochemical inspection and constituent-of-blood checking, and the blood which had to inspect using the plasma which added the anticoagulant into blood, therefore was extract d must be processed etc.
[0004] this invention was made in view of such a conventional fault, and the purpose is measuring the concentration of the matter which produces the antigen-antibody reaction in the blood using the sam sample as using for constituent-of-blood inspection, without carrying out centrifugal separation of th xtracted blood.
[0005]
[Means for Solving the Problem] In the measuring method of the antigen-antibody reaction matter which measures the predetermined antigen in the blood which extracted invention of a claim 1, or the concentration of an antibody A surfactant is poured in and agitated into the extracted blood. into this liquid A stabilizing agent, After the antibody or antigen to the buffer solution, the aforementioned predetermined antigen, or an antibody pours in and agitates the latex liquid by which sensitization was carried out, light is irradiated at this liquid and it is characterized by measuring the aforementioned predetermined antigen in the aforementioned blood, or the concentration of an antibody based on the amount of transmitt d lights.
[0006] Invention of a claim 2 is characterized by a predetermined antigen being C reactivity protein in invention of a claim 1.
[0007] In th measuring device f the antig n-antibody reaction matter which measures the predetermined

antigen in the blood which extracted inv ntion of a claim 3, or the concentration of an antibody A pouring means to pour each of the latex liquid with which sensitization of the antibody or antigen to a surfactant, a stabilizing agent, the buffer solution, the aforementioned predetermined antigen, or an antibody was carried out to the blood in the container which holds the extracted blood, and this container in, A churning means to agitate the liquid in the aforementioned container, and an optical irradiation means to irradiate light at the liquid in the afor mentioned container, It is charact rized by providing an amount detection means of transmitted lights to detect the amount of transmitted lights which penetrated the liquid among the light by this optical irradiation means, and a density measurement means to ask for the aforementioned pr determined antigen in the aforementioned blood, or the concentration of an antibody based on the light which this amount detection means of transmitted lights detected.

[0008] Invention of a claim 4 is characterized by a predetermined antigen being C reactivity protein in invention of a claim 3.

[0009]

[Embodiments of the Invention] Drawing 1 shows the spectrophotometer used for this measuring method. Explanation of this equipment sets up the light of the light source 1 so that a spectrum may be carried out with a spectroscope 2, among these the light of wavelength with very little absorption may be irradiated by the sample cell 3 to hemoglobin etc. The sample cell 3 is created by the transparent member, and the light which penetrated this sample cell 3 is changed into an electrical signal with a detector 4. The output of this d t ctor 4 is Log. It results in a converter 5, logarithmic transformation is carried out here, and, next, it is A/D. It results in a converter 6, and is changed into digital value here, and the value is displayed with a drop 7.

[0010] The gestalt of this operation explains how to measure the concentration in blood of a certain matter X which produces an antigen-antibody reaction.

[0011] A tester holds first what mixed the blood and the surfactant which were extracted to the sample cell 3, and was agitated. Blood hemolyzes with this surfactant. That is, the hemoglobin contained in the rythrocyte here is eluted.

[0012] Next, a tester pours in and agitates a stabilizing agent and the buffer solution to a sample cell 3. And a tester performs blank measurement. That is, a tester makes the liquid in this sample cell 3 befor producing an antigen-antibody reaction absorb the light from a spectroscope 2, and checks whether the display of a drop 7 showed the predetermined value and is stable.

[0013] If it checks that the above-mentioned display is stable, a tester will pour into a sample cell 3 the sensitization latex liquid which produces an antigen-antibody reaction to Matter X, and will agitate it.

[0014] The sensitization latex (latex which combined the antibody or the antigen) distributed to the rose ros at this time is condensed by the antigen-antibody reaction, and the particle size on appearance increases. If an aggregate grows and sees with advance of an agglutination reaction and the upper particle size increases, the amount of transmitted lights will decrease. The grade of the particle-size increase by such latex agglutination reaction is decided by concentration of the antigen contained in a sample, or an antibody. Therefore, it depends for the amount of transmitted lights on the concentration of the antigen contained in a sample, or an antibody (7 or inspection, technology, vol.12, and no. 1984 7 moons, the 34th lin reference of the 583rd page right column lowest line - 584th page left column).

[0015] Next, a tester makes this sample cell 3 penetrate the light from a spectroscope 2, reads th display of a drop 7 immediately, reads the display of a drop 7 in this time a in b at the time after predetermined-time t1 progress further, and records each value. The amounts Ita and Itb of transmitted lights at each time by this Opposite numeric values LogIta and LogItb It is obtained.

[0016] absorbance A since it is expressed with A=Log (Io/It) when the amount of incident lights is set to Io and the amount of transmitted lights is generally set to It -- the amount of transmitted lights -- Ita from -- Itb the time of changing -- change part deltaA of the absorbance deltaA=Log (Ita/Itb) =LogIta-LogItb can be calculated and calculated.

[0017] Next, a t ster is deltaA for which it asked with reference to the calibration curve of the matter X in which the r lation of the changed part and concentration of an absorbanc is shown. It asks for corresponding concentration.

[0018] The concentration of Matter X differs here instead of the blood in which the calibration curve carried out [above-mentioned] extraction, r spectively. n sorts of blood serums, i.e., n sorts of standard solutions, each concentration of whose is known It is a changed part deltaA1 of an absorbance like the

above. d ltaA2, deltaA3 .... If deltaAn is calculated and this creates the regr ssion line of the relation of the changed part and concentration of an absorbance, it can ask like drawing 2 .
[0019] In the above-mentioned example, it is asking for the concentration of Matter X directly with reference to the calibration curve from deltaA for which it asked by transmitted light measurement of a whole blood. However, this calibration curve is created based on the standard solution of a blood serum. And the concentration of the matter X in a whole blood (the erythrocyte is included) is thinner than the concentration of the matter X in a blood serum (the erythrocyte is not included). For this reason, if it asks for the concentration of Matter X directly with reference to the above-mentioned calibration curve from the above-mentioned deltaA, some error will arise with the concentration of the actual matter X. Then, this deltaA is amended, and it changes into the value corresponding to the concentration of the matter X in a blood serum, and asks for the concentration of Matter X with reference to the above-mentioned calibration curve using this value. The following relational expression using the hematocrit HCT which measured beforehand and was calculated performs this amendment.
(deltaA after amendment) =deltaAx {100/(100-HCT)} -- (1)
If it does in this way, accuracy can be asked more for the concentration of Matter X.
[0020] When asking for the CRP concentration in blood using the above-mentioned method, the reagent and quantity from which a suitable result is obtained, and light wave length are described below.
[0021] The standard solution for reagent (1) calibration-curve creation; ERUPIA ace CRP reference standard 0, 1.5, 3.5, 7.0, 14.0 mg/dl (die noise TRON company make, tradename)
(2) Latex liquid, a stabilizing agent; ERUPIA ace CRP-L (kit) (die noise TRON company make, tradename) latex liquid; -- anti-Homo sapiens CRP sensitization latex stabilizing-agent; -- bovine-serum-albumin content tris-HCl buffer (3) buffer-solution; -- common buffer and 0.9%NaCl content buffer-solution (4) surfactant; -- a sodium lauryl sulfate [an anionic(-) surfactant]
[0022] Quantity (rate of a volume ratio)
a surfactant 1 -- receiving -- a whole-blood sample -- 10-70 -- in addition according to the amount of a stabilizing agent and the whole-blood sample used about the addition of the buffer solution, it adds suitably

[0023] Conversion becomes it bad that a whole-blood sample is ten or less to a surfactant 1, and hemolysis stops working or more by 70. Moreover, a suitable result will be obtained if the above-mentioned operating wavelength is about 800-1000nm of near-infrared light.
[0024] The example of a time change of an absorbance in case a sample differs from measurement conditions in drawing 3 as reference here is shown. Reaction curves 1 and 2 are the reactions at the tim of using plasma for a sample. Reaction curves 3 and 4 are the reactions at the time of using a whole blood for a sample. Reaction curves 5 and 6 are the reactions at the time of using a whole blood and a surfactant for a sample. Measurement uses three kinds of these samples, and is the 1st reaction first. Sample + buffer-solution + stabilizing agent The absorbance was measured and it checked that an absorbance was fixed. 1, 3, and 5 of a reaction curve are it. That is, it is shown that pass through any sample and the reaction is not progressing with the time. Next, latex liquid was added in each solution as the 2nd reaction, change of an absorbance was observed, and the existence of an antigen-antibody reaction was evaluated. 2, 4, and 6 of a reaction curve are it. It is a reactivity by the method currently performed conventionally uses plasma, and, as for a reaction curve 2, it turns out that the absorbance is increasing with tim . A reaction curve 4 shows that the reaction is not progressing at all by the whole blood. A reaction curve 6 is what added the surfactant to the whole blood, and it turns out that the absorbance is increasing with tim . And if the reaction curve 2 by the conventional method is compared with the reaction curve 6 by the method of this invention, although conversion will fall from the former in the latter, it turns out that both approximate. However, since the concentration of CRP in a whole blood is thinner than CRP in plasma, change part deltaAbs2 of the absorbance when using the plasma of a reaction curve 2 by the above-mentioned (1) formula and the same following formula, when it was an amendment, and change part deltaAbs6 of th absorbance when using the whole-blood + surfactant of a reaction curve 6 serve as the almost same value using the hematocrit HCT measured independently.
(deltaAbs6 after amendment) =(deltaAbs6 when using whole-blood and surfactant) x {100/(100-HCT)}
here -- absorbance of absorbance-0sec of deltaAbs6=300sec it is .
[0025] Although th above is the example of CRP measurement, if the antig n or antibody combined with the lat x particle of latex liquid is replaced with, C reactivity protein [in blood] (it is called below C-

ReactiveProtein; CRP), rheumatoid factor (RF), and antistreptolysin O (ASO) etc. can be measured similarly.

[0026] Next, the equipment which measur s the concentration in blood of the above-mentioned matter X by such method is explained. The whole composition is shown in drawing 4 .

[0027] As for the light of the light source 11, the light of wavelength with very little absorption is generated to hemoglobin etc., and this light is set up so that a sample cell 12 may irradiate. The sample cell 12 is created by the transparent member, and the light which penetrated this sample cell 12 is changed into an electrical signal with a detector 15. the output of this detector 15 -- alike -- A/D It results in a converter 16, and it is changed into digital value here and made to result in a microcomputer 17.

[0028] If a sample and the surfactant transfer pipet 8 hold the blood and the surfactant which are a sample, respectively and has directions of a microcomputer 17, it will pour into a mixing chamber 9 the liquid chosen according to the directions. Churning equipment 10 is equipment which agitates the liquid held in the mixing chamber 9 according to directions of a microcomputer 17. Transfusion equipment 19 is equipment which supplies the liquid held in the mixing chamber 9 to a sample cell 12 according to directions of a microcomputer 17. If the reagent transfer pipet 13 holds the sensitization latex liquid which produces an antigen-antibody reaction to the stabilizing agent, the buffer solution, and Matter X which are a reagent, respectively and has directions of a microcomputer 17, it will pour into a sample cell 12 the liquid chosen according to the directions. Churning equipment 14 is equipment which agitates the liquid held in the sample cell 12 according to directions of a microcomputer 17. A printer 18 prints the data outputted from the microcomputer 17. A microcomputer 17 is A/D while consisting of input units, such as an interface for delivering and receiving data with an operation, the central processing unit (Following CPU being called) which performs control, the main memory which consists of a ROM and RAM, and the exterior, and a keyboard, and controlling each part of this equipment. The data from a converter 16 are processed. The flow chart of operation of CPU is shown in drawing 5 .

[0029] Operation of this equipment is explained with reference to drawing 5 . It is directed that CPU pours blood and a surfactant into a mixing chamber 9 to a sample and the surfactant transfer pipet 8 (Step 100). Thereby, a sample and the surfactant transfer pipet 8 pour blood and a surfactant into a mixing chamber 9. Next, CPU directs churning to churning equipment 10 (Step 101). Thereby, churning equipment 10 agitates the liquid of a mixing chamber 9 predetermined-time t2. Next, it is directed that CPU transports the liquid of the specified quantity to a sample cell 12 from a mixing chamber 9 to transfusion equipment 19 (Step 102). Thereby, transfusion equipment 19 transports the liquid of the specified quantity to a sample cell 12 from a mixing chamber 9.

[0030] Next, it is directed that CPU pours a stabilizing agent and the buffer solution into a sample cell 12 to the reagent transfer pipet 13 (Step 103). Thereby, the reagent transfer pipet 13 pours a stabilizing agent and the buffer solution into a sample cell 12. Next, CPU directs churning to churning equipment 14 (Step 104). Thereby, churning equipment 14 agitates the liquid of a sample cell 12 predetermined-time t2. Next, the light source 11 is made to emit light and CPU is A/D at that time. It checks whether the absorbance is stabl in the predetermined value with the data from a converter 16 (Step 105), and if it judges that it is stable in the predetermined value, it will progress to Step 106. Here, if it judges that it is not stable in a pred termined value, CPU will progress to Step 111, will output that to a printer 18, and will serve as an end.

[0031] It is directed that CPU pours the above-mentioned latex liquid into a sample cell 12 to the reagent transf r pipet 13 in Step 106. Thereby, the reagent transfer pipet 13 pours latex liquid into a sample cell 12. Next, CPU directs churning to churning equipment 14 (Step 107). Thereby, churning equipment 14 agitates the liquid of a sample cell 12 predetermined-time t2.

[0032] Next, make the light source 11 emit light immediately after this churning, the light source 11 is made to emit light after a predetermined time t3 from the time further, and CPU is A/D at each time. It is based on data from a converter 16, and is deltaA a changed part of the difference of the absorbance at both the times, i.e., an absorbance. It asks (Step 108).

[0033] Next, CPU is deltaA for which it asked at Step 108 with reference to the changed correspondence table of the blood drug concentration of Matter X, and an absorbance which it was beforehand inputted and has been memorized to main memory. It asks for the blood drug concentration of the corresponding matter X (Step 109).

[0034] Next, CPU is deltaA a changed part of the absorbance for which it asked at the data of

concentration for which it asked at Step 109, and Step 108. Data are outputted to a printer 18 (Step 110). A printer 18 prints these data.

[0035] The above-mention d correspondence table is a changed part deltaA1 of the absorbance about two or more sorts of each blood serum liquid each concentration of whose th concentration of Matter X differs instead of the above-mentioned sample, and is known using this equipment beforehand. deltaA2, If it asks for deltaA3 —, sinc the changed regr ssion line of a conc ntration-absorbance will be called for by this, it can create from this straight line.

[0036] with this equipment, it asks for deltaA by transmitted light measurement of a whole blood (Step 108), and asks for the concentration of Matter X directly with reference to a calibration curve from this deltaA -- **** (Step 109) -- after asking for deltaA at Step 108, the above-mentioned (1) formula amends this deltaA, and you may make it ask for the concentration of Matter X with reference to a calibration curve from deltaA after this amendment The hematocrit HCT used for this amendment is calculated by another measurement, and the main memory of a microcomputer 17 is made to memorize it beforehand. If it does in this way, accuracy can be asked more for the concentration of Matter X.

[0037]

[Effect of the Invention] Since according to the method of this invention, and equipment a direct reagent can be poured in and measured to a whole blood in case the concentration of the antigen-antibody reaction matter in blood is measured, it is not necessary to carry out centrifugal separation of the blood. For this reason, the concentration of this kind of matter can be measured quickly. Furthermore, since measurement is possible using the sample which carried out the same processing as constituent-of-blood measurement, it does not take time and effort. Moreover, even if it is an institution without a centrifugal separation machine according to the method of this invention, it can measure.

[Translation done.]

* NOTICES *

1.This document has be n translated by computer. So the translation may not reflect the original precisely.

2.**** shows the word which can not be translated.
3.In the drawings, any words are not translated.

DESCRIPTION OF DRAWINGS

[Brief Description of the Drawings]
[Drawing 1] Drawing showing the composition of the spectrophotometer used for this invention method.
[Drawing 2] Explanatory drawing of calibration-curve creation used for this invention method.
[Drawing 3] Drawing showing a time change of the absorbance of various liquids.
[Drawing 4] Drawing showing the composition of this invention equipment.
[Drawing 5] Drawing for explaining operation of the equipment shown in drawing 4 .
[Description of Notations]
1 11 Light source
3 12 Sample cell
4 15 D tector
7 Drop
8 Sample and Surfactant Transfer Pipet
9 Mixing Chamber
13 Reagent Transfer Pipet
17 Microcomputer
19 Transfusion Equipment

[Translation done.]

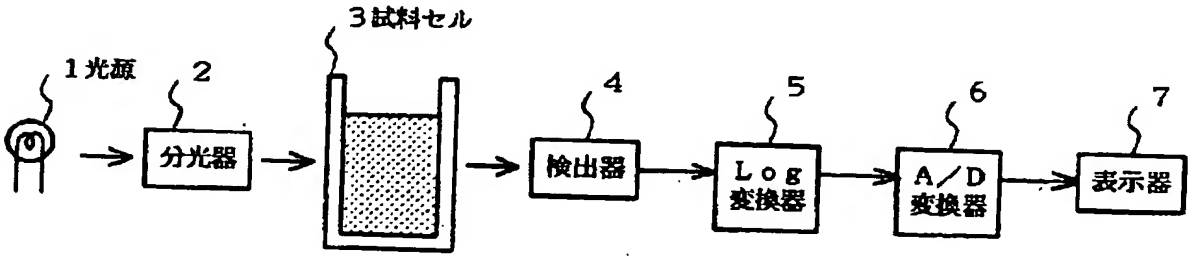
* NOTICES *

1.This document has been translat d by computer. So the translation may not reflect the original precisely.

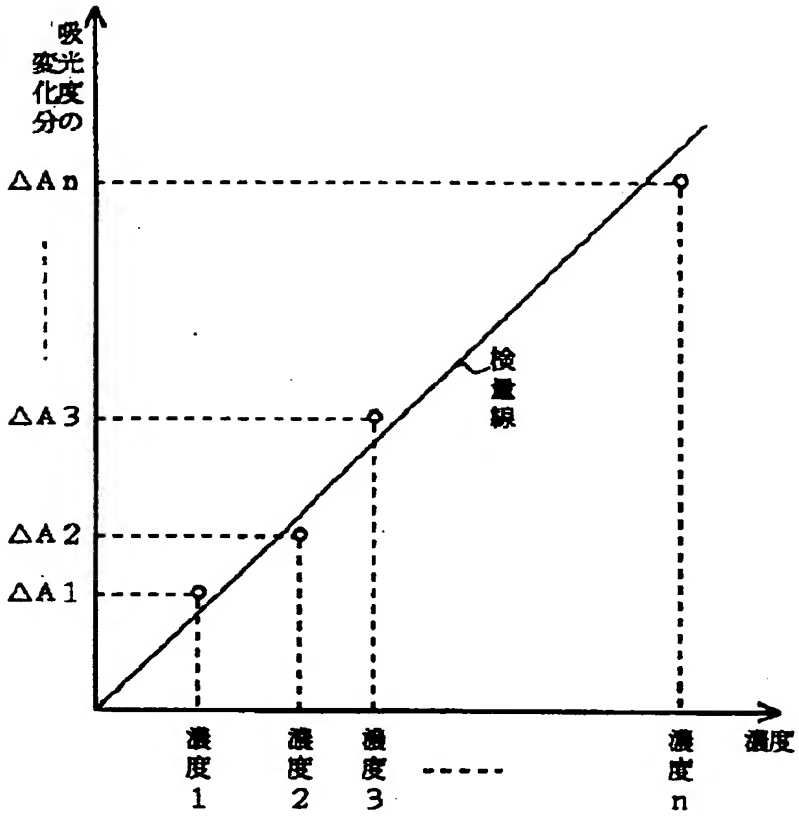
2.**** shows the word which can not be translated.
3.In the drawings, any words are not translated.

DRAWINGS

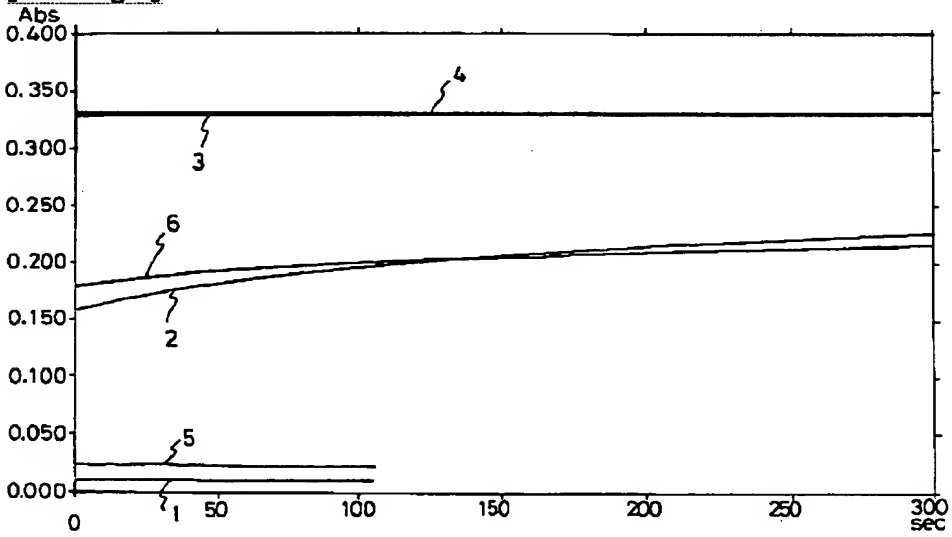
[Drawing 1]



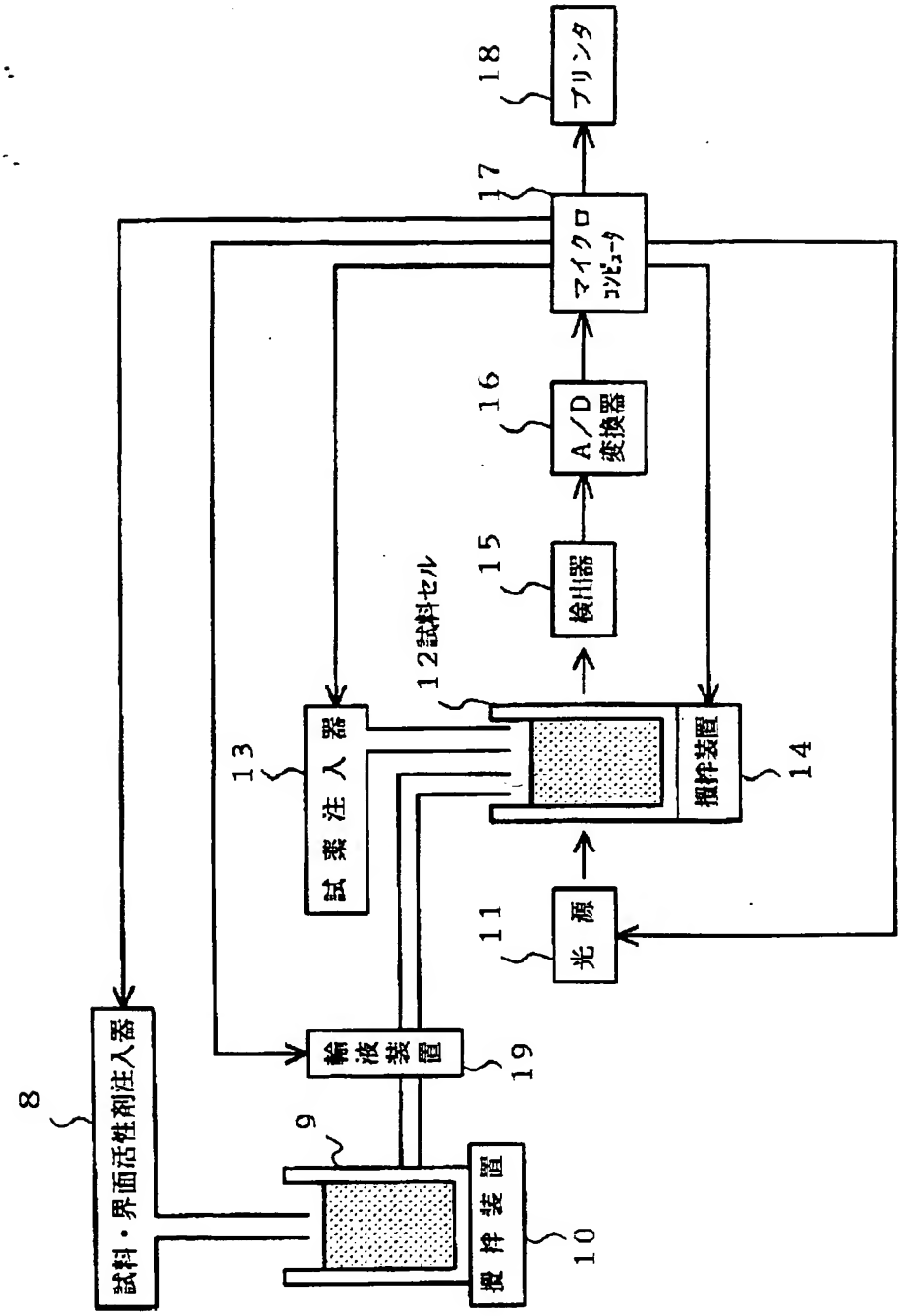
[Drawing 2]



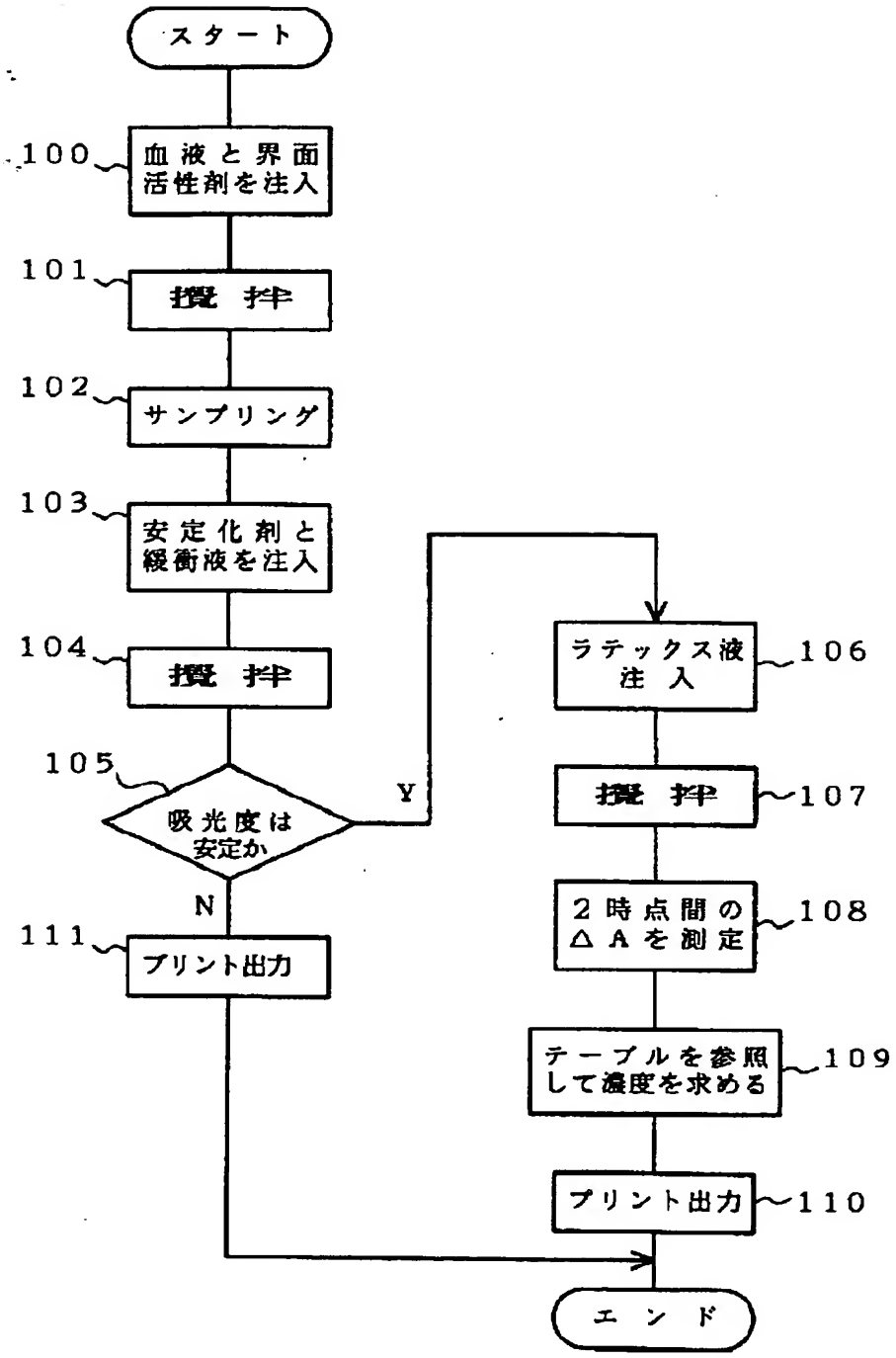
[Drawing 3]



[Drawing 4]


プリンタ
18
マイクロコンピュータ
17
A／D変換器
16
検出器
15
12試料セル
試薬注入器
13
撹拌装置
14
光源
11
輸液装置
19
撹拌装置
10
9
試料・界面活性剤注入器
8

[Drawing 5]



[Translation done.]